UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,192	06/12/2001	Michael U. Walker	PB-0009-1 CIP	7368

27904 7590 01/29/2003

INCYTE GENOMICS, INC.
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
GUNTER, DAVID R	

ART UNIT	PAPER NUMBER
1634	11

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,192	WALKER ET AL.	
	Examiner	Art Unit	
	David R. Gunter	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 13, and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. This action is in response to Amendment B, paper number 10, received November 13, 2002. The amendment has been fully considered and entered. The previous rejections in the office action dated August 8, 2002 (paper number 9) under 35 U.S.C. 101 and 112 are maintained. All of the arguments have been thoroughly considered and are discussed below.

Maintained Claim Rejections - 35 USC § 101 and 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-3 and 13-14 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific utility because the disclosed uses of the polynucleotide are not specific and are generally applicable to any polynucleotide. The specification discloses many potential uses for the polynucleotide including detecting gene expression (page 3, line 4), as a probe (page 12, line 23), and "for expressing mRNA and protein, or conversely to block transcription or translation of the mRNA" (page 14, lines 9-10). These are non-specific uses that are applicable to polynucleotides in general and not particular or specific to the polynucleotide claimed.

Further, the claimed polynucleotide is not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. In this case the polynucleotide is known only to be co-expressed with creatine kinase M (page 24, line 31), and has no asserted or identified specific and substantial utilities. The research contemplated by the applicants to characterize uses for the polynucleotide does not constitute a specific and substantial utility. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Note, because the claimed invention is not supported by a specific and substantial asserted utility for the reasons set forth above, credibility has not been assessed. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the polynucleotides such that another non-asserted utility would be well established for the compounds.

3. Claims 1-3 and 13-14 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments

4. All of the arguments presented and the declaration under 37 CRF 1.132 have been thoroughly considered and are not found persuasive. The applicants assert that the polynucleotide of SEQ ID NO: 41 has a specific, substantial, and credible utility because "*only*

48 novel polynucleotides showed strong expression and association with the known cardiac muscle-associated genes" (page 3, last paragraph). The applicant further asserts that the polynucleotide has "*asserted utility as ... surrogate markers for disorders of cardiac muscle function, and specifically cardiac injury, which were identified by their co-expression with known diagnostic and prognostic markers*" (page 4, first paragraph). The applicant asserts that "*SEQ ID NO: 41 was selected as a representative for the combination and as a surrogate marker for the highly-associated creatine kinase M, a known diagnostic marker for cardiac injury*" (page 4, third paragraph). The declaration by the inventor and the attached journal article asserted the ability of the Guilt By Association (GBA) method to identify correlations between the expression level of known genes and the expression levels of each of a pool of candidate genes. The declaration and references have been thoroughly reviewed, but were not found persuasive for the following reasons.

The examiner did not dispute the ability of the GBA method to identify correlations between the expression level of known genes and expression levels of each of a pool of candidate genes. Nor did the examiner dispute the relationship between detection of Creatine Kinase M (CKM) **protein** in a blood sample and the presence of cardiac injury. The applicant provides three references to support the correlation between detection of CKM **protein** in a blood sample and cardiac injury in the table on page 22 of the specification. Luscher, et al., (Cardiology 89:222-228, 1998) describes "solid-phase chromatographic immunoassay technology to quantitatively detect [CKM] mass ... in whole blood" (page 223, right column, second paragraph). Kost, et al., (Arch Pathol Lab Med 122:245-251, 1998) teaches "[CKM] mass was determined with a sequential chemiluminometric assay" (page 246, left column, third

paragraph). Feng, et al., (Am J Clin Pathol 110:70-77, 1998) also describes measurements of the amount of CKM protein in a blood sample (page71, left column, fourth paragraph).

While the specification and the papers cited by the applicant teach a correlation between cardiac injury and an increase in the level of CKM **protein** in a blood sample, they do not offer any teaching or guidance that demonstrates a correlation between an increased expression level of CKM **mRNA** in tissue samples and cardiac injury. It was known to those of skill in the art at the time the application was filed that there was a poor correlation between cardiac injury and alteration in the expression of CKM mRNA. Mehta, et al. (Circulation Research 63(3):512-517, 1988) induced myocardial ischemia by ligation of the left anterior descending coronary artery and collected myocardial tissue at various time points after the ligation. Mehta demonstrates a brief decrease of about 40% in CKM mRNA expression in the myocardium at 1.5 hours post-ligation, but the CKM mRNA expression returns to normal at 3 hours post ligation (Mehta, page 516, figure 4). Mehta teaches "[t]he mechanism by which [CKM] mRNA decreases is not clear and also it is not understood as to why [CKM] mRNA levels are restored at 6 hours after coronary ligation" (Mehta, page 516, right column, last paragraph).

Schultz, et al., (J Mol Cell Cardiol 29:2665-2673, 1997) surgically induced mitral regurgitation in dogs in order to produce volume overload cardiac hypertrophy (page 2666, left column, third paragraph). RNA was extracted from myocardial tissue (page 2667, right column, fourth paragraph) and the level of expression of CKM was detected. Schultz teaches that "steady state mRNA of [CKM] did not differ" in any of the treatment groups (page 2669, right column, second paragraph).

The applicant has demonstrated that the expression level of the polynucleotide of SEQ ID NO: 41 is correlated to the expression level of the mRNA for CKM in tissue samples. The applicant has further demonstrated that the level of CKM protein present in the blood correlates to cardiac injury. However, the applicant has not provided any teaching or guidance to demonstrate that an increase in the expression level of CKM mRNA corresponds to an increase in the amount of CKM protein present in the blood. As such, the applicant does not provide any teaching or guidance to demonstrate that an increase in the expression level of the polynucleotide of SEQ ID NO: 41 can be correlated to the presence of cardiac injury. Based on the known poor correlation between changes in CKM mRNA expression levels and the presence of cardiac injury as taught by Mehta and Schultz, the skilled artisan would be required to perform additional experimentation to reasonably confirm a real world context of use for the polynucleotide of SEQ ID NO: 41 as a marker for cardiac injury. The utility rejection is therefore maintained and made final.

5. The applicant asserts that they "have provided sufficient evidence to clearly demonstrate that the 35 U.S.C. 101 utility requirement has been satisfied," and therefore request that the rejection under 35 U.S.C. 112, first paragraph be withdrawn. As described above, the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, and therefore one skilled in the art clearly would not know how to use the claimed invention.

To determine a real world use for the polynucleotide, the skilled artisan would be required to perform undue experimentation as the art provides conflicting teaching regarding the

correlation between the expression of CKM mRNA and the presence of cardiac injury. Therefore, for the reasons set forth in the 101 rejection and the response to arguments, as well as for the reasons set forth in the previous office action, the rejection under 35 U.S.C. 112, first paragraph is maintained.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David R. Gunter whose telephone number is (703) 308-1701. The examiner can normally be reached on 9:00 - 5:00 M - F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 746-9212 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

David R. Gunter, DVM, PhD
January 22, 2003

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600